CASE REPORT

Femoral–facial syndrome in an infant of a diabetic mother

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SUMMARY

Femoral–facial syndrome (FFS) is a very rare multiple congenital anomaly syndrome. The authors describe a case of FFS in a 2-day-old infant of a diabetic mother. The phenotypic features include bilateral symmetrical femoral involvement with completely aplastic right-sided femur, severely hypoplastic left femur and unusual facial dysmorphic features without other skeleton/spinal and genitourinary anomalies. Cases of FFS need to be carefully evaluated because of the similarity between FFS and caudal dysgenesis, a condition frequently related to maternal diabetes and with other syndromes characterised by femoral hypoplasia and associated anomalies, which can pose a diagnostic challenge.

BACKGROUND

Femoral–facial syndrome (FFS; OMIM 134780),¹ (formerly called femoral hypoplasia-unusual facies syndrome), is a very rare multiple anomaly syndrome of unknown aetiology comprised of unusual facial features, which include upward-slanting palpebral fissures, low set poorly formed pinnae, short nose, long philtrum, micrognathia, bilateral aplasia/hypoplasia of the femur and humeroradial synostosis, and involvement of other systems such as the cardiovascular, genitourinary and central nervous system. First delineated by Daentl *et al*² in 1973, it is a syndrome of unknown aetiology. FFS is more common in females, and the majority of cases are sporadic. An autosomal dominant inheritance has been described in two families,^{3 4} and autosomal recessive inheritance has been suggested in one family.⁵ Similar cases have been reported by Shawky *et al*⁵ from Egypt, and Sabry *et al*⁶ from Kuwait. To the best of our knowledge, this is the first case reported from Saudi Arabia.

CASE PRESENTATION

The proband, a 2-day-old infant of Saudi Arabian origin, was born at term by caesarean section to a 39-year-old gravida 8, para 6, aborts 1, mother after an uncomplicated pregnancy. The mother is not a known diabetic; she presented for her first obstetric visit at the end of the first trimester. Routine evaluation revealed hyperglycaemia and glycated hemoglobin (HbA1c) of 8.9%. Insulin injection was started, which the mother continued throughout the pregnancy. Her glycaemic control was poor during the first trimester, but her subsequent HbA1c showed good glycaemic control. The first antenatal scan performed during the 19th week of gestation was reported to be normal.

The woman did not appear for a follow-up scan. The family history was unremarkable for type 2 diabetes mellitus on both sides of the mother's family. The mother was not related by blood to the proband's father, and there was no history of exposure to other teratogens. The birth weight was 3.5 kg (on 50th centile), length was 42 cm (below 0.4th centile) and occipitofrontal circumference was 35 cm (on 50th centile). Other anthropometric measurements were within normal limits.

Dysmorphological examination revealed sparse and broad eyebrows, upward slanting of palpebral fissures, telecanthus, a short nose with a broad tip, prominent cheeks, a long philtrum, a thin upper lip, microretrognathia and a short neck (*figure 1A*).

Physical examination of the lower limbs showed bilateral symmetrical femoral shortening (*figure 1B*). There was overlapping of the left foot toes, second over third and fourth over third (*figure 1C*). Upper limb, spine, skin, genitalia and neurological examination were within normal parameters. The remainder of the physical examination was unremarkable and the baby was otherwise healthy and active.

INVESTIGATIONS

Complete blood count, urea and electrolytes, liver enzymes, blood sugar, coagulation profile and thyroid function test were all within normal limits. Echocardiogram showed a tiny patent ductus arteriosus. Abdominal ultrasound was unremarkable. Chromosomal analysis was reported as 46, XY at band 500 resolution.

Radiologically, the right leg revealed a completely aplastic right femur, a severely hypoplastic left femur (*figure 2*), bilateral hypoplastic acetabulum and bilateral absent patellae.

DIFFERENTIAL DIAGNOSIS

Lower limb defects, unilateral/bilateral with or without upper limb involvement, may be of syndromic, isolated or environmental causes. Physical examination of patients should include a thorough search for associated anomalies, especially of the spine, to rule out:

- ▶ Caudal dysgenesis,
- ▶ Proximal focal femoral hypoplasia.

DISCUSSION

We presented a case of an infant with the characteristic features of FFS, born to a diabetic mother. FFS has a strong association with maternal diabetes, and maternal hyperglycaemia is one of the

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Figure 1 (A) Sparse and broad eyebrows, upward slanting of palpebral fissures, telecanthus, a short nose with a broad tip, prominent cheeks, a long philtrum, a thin upper lip, microretrognathia and a short neck. (B) Bilateral symmetrical femoral shortening. (C) Overlapping of the left foot toes, second over third and fourth over third, is seen.

strongest human teratogens.⁷ Most of the congenital malformations occurring in infants of diabetic mothers are blastogenic in origin,⁴ which can result in a significantly higher risk for congenital malformations including neural tube defects, caudal dysgenesis, congenital heart defects, renal anomalies and femoral hypoplasia. The incidence of maternal diabetes among FFS cases was 28–38%.^{8–9}

While complete absence of the femur is a very rare finding in FFS,^{8–9} humeroradial synostosis and limitation of elbow movements are frequently reported.^{8–10} Congenital heart defects occur with increasing frequency in FFS,^{8–9–11} and many reported cases have been associated with genitourinary^{6–9} and central nervous system anomalies.¹²

Daentl *et al*² described four cases of FFS in unrelated individuals who were born to non-diabetic mothers. However, in their elegant study, Burn *et al*⁸ presented a series of 13 patients, of whom 6 had features compatible with the diagnosis of FFS and 3 were associated with maternal diabetes, as in the cases of

Johnson *et al*.⁹ Similarities to caudal dysgenesis were pointed out by Gleiser *et al*.¹⁰ An important association between maternal diabetes and caudal dysplasia exists, and the frequency of maternal diabetes in this condition has been reported to be 16%. Many features of caudal regression syndrome (Caudal Dysgenesis) overlap with FFS,^{10–13} however, the facial dysmorphic features in FFS are an important clue to differentiate this condition from caudal dysplasia.

FFS can present with or without typical facial features or with minimal bony involvement, which makes it difficult to differentiate from proximal focal femoral hypoplasia.¹⁴

Learning points

- ▶ Serial prenatal sonographic evaluation with three-dimensional imaging should be carried out by experienced obstetricians and sonologists in diabetic mothers, to delineate skeleton malformations in general and the diagnosis of femoral–facial syndrome in particular.
- ▶ Accurate clinical diagnosis is crucial for prognostication, for identifying further health issue and for accurate genetic counselling.
- ▶ Careful monitoring and good glycaemic control during early pregnancy are strongly recommended to reduce the frequency of serious malformations due to maternal diabetes to a level similar to that of non-diabetic women.

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Competing interests None declared.

Patient consent Obtained.

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Figure 2 Completely aplastic right femur, a severely hypoplastic left femur (arrow), bilateral hypoplastic acetabulum, and bilateral absent patellae.

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